

IN THE CLAIMS

Please amend claims 3 to 8, 10 to 23, and 62 to 64, as follows:

*NE.* At line 1 of each claim, after "human" but before "antibody," please insert --monoclonal--.

REMARKS

In the Response and Amendment filed December 9, 2002, Applicants elected Group I, claims 1 to 29, for prosecution in the subject application. Applicants additionally canceled claims 2 and 9 without prejudice and added new claims 62 to 64, which depend from claim 1. In the present Supplemental Amendment, claims 3 to 8, 10 to 23, and 62 to 64 have been amended to address an informality as set forth below. A copy of the claims following entry of the present Supplemental Amendment and the Response and Amendment filed December 9, 2002, is attached herewith.

Regarding the Amendments

The amendments to claims 3 to 8, 10 to 23, and 62 to 64 were made to address an informality. In particular, the amendment to the claims to recite "monoclonal" was made to conform these claims with claim 1, which was amended to recite "monoclonal" in the Response and Amendment filed December 9, 2002. Thus, as the amendments were made to address an informality, no new matter is added and entry thereof is respectfully requested.

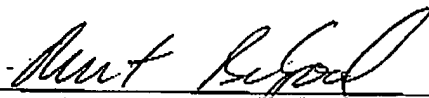
### CONCLUSION

Applicants respectfully request entry of the present Supplemental Amendment and substantive examination of the application. If the Examiner would like to discuss any of the issues raised in the response and amendment, Applicant's representative can be reached at (858) 509-4065.

Please charge any additional fees, or make any credits, to Deposit Account No. 03-3975.

Respectfully submitted,

Date: 1-7-03

  
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**Clean Claims Upon entry of the present Supplemental Amendment and the Response and  
Amendment filed December 9, 2002**

- Sub C1*
1. A human monoclonal antibody or fragment thereof that specifically binds to human CD40.
  3. The human monoclonal antibody of claim 1, wherein the antibody is produced by a hybridoma cell line or subclones thereof, and wherein the antibody is denoted as no. 11 or 72, or the hybridoma is denoted as F1-102, F5-152, F2-103, F5-77, F5-157 or F4-465.
  4. The human monoclonal antibody of claim 1, wherein the antibody has the CD40 binding specificity of the antibody denoted as no. 11 or 72, or the antibody produced by the hybridoma denoted as F1-102, F5-152, F2-103, F5-77, F5-157 or F4-465.
  5. The human monoclonal antibody of claim 1, wherein the antibody has a CD40 modulating activity of the antibody denoted as no. 11 or 72, or the antibody produced by the hybridoma denoted as F1-102, F5-152, F2-103, F5-77, F5-157 or F4-465.
  6. The human monoclonal antibody fragment of claim 1, wherein the fragment comprises an scFv, Fab, Fab', or F(ab')<sub>2</sub> fragment.
  7. The human monoclonal antibody fragment of claim 6, wherein the fragment comprises a fragment of the antibody denoted as no. 11 or 72, or the antibody produced by the hybridoma denoted as F1-102, F5-152, F2-103, F5-77, F5-157 or F4-465.
  8. The human monoclonal antibody of claim 1, wherein the antibody is detectably labeled.
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- Sub C2*
10. The human antibody of claim 1, wherein the antibody decreases binding of a CD40 ligand to CD40.
  11. The human monoclonal antibody of claim 1, wherein the antibody increases binding of a CD40 ligand to CD40.
  12. The human monoclonal antibody of claim 1, wherein the antibody decreases a CD40 activity.
  13. The human monoclonal antibody of claim 12, wherein the antibody contains a lambda light chain sequence.
  14. The human monoclonal antibody of claim 12, wherein the antibody decreases proliferation of a cell expressing CD40.
  15. The human monoclonal antibody of claim 14, wherein the cell is a B-cell.

Sub  
C1  
B2

16. The human monoclonal antibody of claim 12, wherein the antibody decreases expression of a protein.
17. The human monoclonal antibody of claim 16, wherein the protein comprises CD95, CD80 or CD86.
18. The human monoclonal antibody of claim 1, wherein the antibody increases a CD40 activity.
19. The human monoclonal antibody of claim 18, wherein the antibody increases proliferation of a cell expressing CD40.
20. The human monoclonal antibody of claim 19, wherein the cell is a B-cell.
21. The human monoclonal antibody of claim 18, wherein the antibody increases expression of a protein.
22. The human monoclonal antibody of claim 21, wherein the protein comprises CD95, CD80 or CD86.
23. The human monoclonal antibody of claim 1, further comprising a pharmaceutical formulation.

Sub  
C1

24. A host cell that expresses the antibody of claim 1.
25. A nucleic acid that encodes the antibody of claim 1.
26. A host cell containing the nucleic acid of claim 25.
27. A method of producing a human CD40 antibody that modulates an activity of CD40 comprising:
  - (a) administering CD40 or an immunogenic fragment thereof to a mouse capable of expressing human immunoglobulin;
  - (b) screening the administered mouse for expression of a human CD40 antibody;
  - (c) selecting a mouse that produces a human CD40 antibody;
  - (d) isolating an antibody from the mouse that produces a human CD40 antibody; and
  - (e) determining whether the human CD40 antibody modulates an activity of CD40 thereby producing a human CD40 antibody that modulates an activity of CD40.
28. A method of producing a human CD40 monoclonal antibody that modulates an activity of CD40; comprising:

- Sub C1
- (a) administering human CD40 or an immunogenic fragment thereof to a mouse capable of expressing human immunoglobulin;
  - (b) isolating spleen cells from the mouse that produces a human CD40 antibody;
  - (c) fusing the spleen cells with a myeloma cell to produce a hybridoma; and
  - (d) screening the hybridoma for expression of a human CD40 antibody that modulates an activity of CD40 thereby producing a human monoclonal CD40 antibody that modulates an activity of CD40.

29. A monoclonal antibody isolated from a hybridoma produced by the method of claim 28.

- Sub C1 BB
- 62. The human monoclonal antibody or fragment of claim 1, wherein the antibody inhibits CD95 expression of Ramos B cells mediated by CD40 ligand in vitro, in the condition of 1 µg/ml of soluble CD40 ligand and 1 µg/ml of the antibody.
  - 63. The human monoclonal antibody or fragment of claim 1, wherein the antibody inhibits human B-cell proliferation mediated by CD40 ligand in vitro, in the condition of 1 µg/ml of soluble CD40 ligand and 10 nanogram/ml of the antibody.
  - 64. The human monoclonal antibody or fragment of claim 62 or 63, wherein the antibody has a Kd value of 0.8 to 4 nM, as determined by BiaCore® analysis.